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U. S. ARMY MEDICAL RESEARCH & NUTRITION LABORATORY

INFLUENCE OF ORALLY ADMINISTERED ANTIBIOTICS ON GROWTH AND PLASMA LIPID LEVELS OF GROWING CHICKS

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U. S. ARMY MEDICAL RESEARCH AND NUTRITION LABORATORY
FITZSIMONS GENERAL HOSPITAL
Denver 40, Colorado

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Report of

INFLUENCE OF ORALLY ADMINISTERED ANTIBIOTICS ON GROWTH AND PLASMA LIPID LEVELS OF GROWING CHICKS

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INFLUENCE OF ORALLY ADMINISTERED ANTIBIOTICS ON GROWTH AND PLASMA LIPID LEVELS OF GROWING CHICKS

OBJECT:

To determine the influence of orally administered antibiotics on plasma lipids of growing chicks.

SUMMARY:

Growing chicks were fed semi-purified diets supplemented with antibiotics or sulfa drugs in the presence or absence of supplemental cholesterol.

The data indicate that antibiotics and sulfa drugs depress plasma cholesterol levels of chicks fed a cholesterol-free diet when they also stimulate growth, but are without effect in the absence of such a growth stimulation. In cholesterol-fed chicks, antibiotics and sulfasuxidine elevated plasma cholesterol and lipid phosphorus levels.

A highly significant positive correlation was observed between plasma cholesterol and lipid phosphorus levels for chicks fed either a cholesterol-free or supplemented diet.

APPROVED:

Marion E. McDowell

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Lt. Colonel, MC
Director

INTRODUCTION

Recent studies have demonstrated an effect of dietary antibiotics on serum cholesterol levels. Nelson et al. (9) observed that the addition of chlortetracycline to a commercial ration resulted in increased serum cholesterol and lipids in rabbits. Goldberg and Smith (1), employing a low-fat and a 12.5% cottonseed oil diet, reported that chlortetracycline resulted in a slight increase in the plasma cholesterol level of rabbits receiving the low-fat diet as compared to a decrease in serum and tissue cholesterol of animals receiving the cottonseed oil ration.

The type of carbohydrate fed also appears to influence the effect of antibiotics and sulfa drugs on serum cholesterol levels. Portman et al. (10) reported that succinylsulfathiazole did not alter the serum cholesterol of rats receiving a sucrose diet, but elevated the serum cholesterol levels of rats fed a starch-containing diet. Kritchevsky et al. (5) found elevated cholesterol levels in chicks fed cholesterol when the diet contained glucose as the carbohydrate source, but not when sucrose replaced glucose.

Recently, Howe and Bosshardt (3, 4) have studied the effect of oxytetracycline, chlortetracycline and succinylsulfathiazole on plasma cholesterol in the mouse. These authors found an elevation in plasma cholesterol when oxytetracycline and succinylsulfathiazole were fed in a diet containing saturated fat, cholesterol and cholic acid. When an unsaturated fat replaced the saturated fat, oxytetracycline was without effect. Chlortetracycline under similar conditions depressed plasma cholesterol. In diets without added cholesterol, chlortetracycline produced lowered cholesterol levels only in the presence of highly unsaturated fat such as cod liver oil and had no effect in the presence of less highly unsaturated fats such as corn oil.

In human subjects, Samuel and Steiner (12) reported a hypocholesteremic effect for neomycin. More recently, Steiner et al. (13) have shown that intramuscularly administered neomycin failed to influence serum cholesterol levels in atherosclerotic patients, and concluded that oral neomycin depresses serum cholesterol through a local effect on the gastrointestinal tract. The hypocholesterolemic effect of oral neomycin has been corroborated (11) and evidence has been presented which indicates that the effect of neomycin is mediated by impairing lipid absorption (8).

The data to be presented indicate that plasma cholesterol levels of growing chicks are not influenced by antibiotics except in situations where they also have a growth-stimulating effect.

EXPERIMENTAL

Male Hy-Line chicks were used in two experiments. The chicks were fed a commercial diet for one week prior to receiving the experimental diets. The experimental period was of three weeks' duration in experiment I and four weeks in experiment II.

The chicks were housed in heated cages having raised wire floors. The composition of the basal diet used for both experiments is shown in Table 1; the design of each experiment is indicated in the tables of results (Tables 2 and 3).

At the termination of the experimental period, blood samples were obtained by cardiac puncture using heparin as an anticoagulant. The blood was centrifuged and the plasma taken for cholesterol, and in experiment II, for lipid phosphorus analysis. Cholesterol and lipid phosphorus were determined by previously described procedures (7).

RESULTS

All the antibiotics fed in experiment I with the exception of oxytetracycline stimulated growth significantly (Table 2); oxytetracycline also stimulated growth, but the difference was not statistically significant. All the treatments employed did, however, significantly depress plasma cholesterol levels.

In experiment II, penicillin, neomycin and sulfasuxidine did not influence growth or plasma lipid levels of chicks fed a cholesterol-free diet. In the cholesterol-supplemented groups, however, growth was depressed by neomycin and sulfasuxidine, and plasma cholesterol and lipid phosphorus were elevated by all treatments.

In Figures 1 and 2 are presented the relationship between plasma cholesterol and lipid phosphorus of chicks fed a cholesterol-free and supplemented diet, respectively. In both cases, a highly significant ($P < 0.01$) correlation between these parameters was observed, the correlation coefficients being + 0.68 and + 0.88 for the cholesterol-unsupplemented and supplemented groups, respectively.

DISCUSSION

The results obtained in the two experiments for chicks fed a cholesterol-free diet are not in agreement. In experiment I, antibiotics depressed plasma cholesterol while in experiment II they were ineffective. The response in experiment I can probably be related to the growth stimulation. It has been demonstrated previously that low-protein diets and amino acid-deficient diets

which depress growth also elevate plasma cholesterol (7). The growth-stimulating effects of antibiotics are generally only evident in animals housed in unclean quarters or suffering from subclinical infections (2). The growth stimulation resulting from antibiotic feeding in experiment I might very well indicate the presence of such a mild infection which was absent in experiment II.

The hypercholesterolemic effect of the antibiotics and sulfa drug fed in experiment II is in accord with findings in cholesterol-fed rabbits (9). The effect of neomycin is in contrast to its hypocholesterolemic effect in the human (12). Further studies are necessary to gain a better understanding of the mechanism of action of antibiotics in altering blood lipids.

The correlation observed between plasma cholesterol and lipid phosphorus levels is in accord with a previous report (6). These data show a much slower increase in the cholesterol:phospholipid ratio with increasing plasma cholesterol levels in chicks fed the cholesterol-free diet than in the cholesterol-fed chick. The increase in lipid phosphorus accompanying plasma cholesterol levels can be interpreted to represent a homeostatic mechanism which the animal appears capable of maintaining in an endogenous hypercholesterolemia. However, in an exogenous hypercholesterolemia resulting from cholesterol feeding, the increase in cholesterol level is so great and rapid that the animal cannot maintain the constancy of the cholesterol: lipid phosphorus ratio.

ACKNOWLEDGMENTS

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TABLE 1

Composition of Basal Diet

Ingredient	gm/100 gm diet
Yellow corn meal	34.26
Soybean oil meal	30.84
DL-methionine	0.30
Corn oil	3.00
Salt mixture[1]	4.00
Vitamin mixture[2]	0.40
Choline Cl	0.20
Glucose	to 100.00

[1] Chick salt mixture, supplied per kg of diet when fed at the rate of 5.31% of the diet: (in grams) $CaCO_3$, 3.0; $Ca_3(PO_4)_2$, 28.0; K_2HPO_4, 9.0; $MgSO_4$, 1.25; Fe gluconate, 2.24; NaCl, 8.80; and (in milligrams) $ZnSO_4 \cdot 7H_2O$, 60; KI, 40; $CuSO_4$, 20; H_3BO_3, 9; $CoSO_4 \cdot 7H_2O$, 1; $MnSO_4$, 650.

[2] Chick vitamin mix, supplied in mg/kg of diet when fed at the rate of 0.40% of the diet; thiamine.HCl, 25.0; riboflavin, 16.0; Ca pantothenate, 20.0; pyridoxine, 6.0; biotin, 0.6; folic acid, 4.0; p-aminobenzoic acid, 2.0; menadione, 5.0; and vitamin B_{12}, 20 µg; inositol, 100; ascorbic acid, 250; niacin, 150; vitamin A, 10,000 IU; vitamin D_3, 1,000 ICU; α-tocopheryl acetate, 100 mg.

TABLE 2

Influence of Orally Administered Antibiotics on Weight Gain and Plasma Cholesterol Level of Chicks

Experiment I

Supplement	Level fed	Body weight gain[1]	P value[2] compared to control	Plasma cholesterol	P value[2] compared to control
	per kg of diet	gm		mg/100 ml	
None		226 ± 16[3]		164 ± 25[3]	
Penicillin G	2,000 units	247 ± 25	< 0.05	112 ± 15	< 0.01
Oxytetracycline.HCl	300 μgm	243 ± 36	NS[2]	126 ± 15	< 0.01
Chlortetracycline	600 μgm	266 ± 28	< 0.01	123 ± 18	< 0.01
Neomycin SO_4	2.0 mg	256 ± 32	< 0.02	141 ± 15	< 0.05
Succinylsulfathiazole	10 gm	264 ± 25	< 0.01	140 ± 15	< 0.02

1 Weight gain from 7th to 28th day of age.

2 Probability (P) of values being different from unsupplemented control group; $P > 0.05$ taken as not significant (NS).

3 Mean for 10 chicks ± standard deviation.

TABLE 3

Influence of Orally Administered Antibiotics on Weight Gain and Plasma Lipids of Chicks Fed Diets Containing or Free of Cholesterol

Experiment II

Supplement	Body weight gain[2] gm	Body weight gain[2] P value[3]	Plasma cholesterol mg/100 ml	Plasma cholesterol P value[3]	Plasma lipid phosphorus mg/100 ml	Plasma lipid phosphorus P value[3]
No added cholesterol						
None	317 ± 27[4]		176 ± 21[4]		13.3 ± 1.3[4]	
Penicillin G	266 ± 22	< 0.01	190 ± 26	NS	13.4 ± 2.6	NS
Neomycin SO_4	316 ± 26	NS	187 ± 30	NS	11.7 ± 2.4	NS
Sulfasuxidine	312 ± 31	NS	185 ± 17	NS	14.0 ± 1.2	NS
2% cholesterol added						
None	334 ± 26		463 ± 101		11.6 ± 1.7	
Penicillin G	358 ± 28	NS	675 ± 245	< 0.05	16.0 ± 2.8	< 0.01
Neomycin SO_4	300 ± 33	< 0.05	676 ± 178	< 0.02	15.8 ± 2.3	< 0.01
Sulfasuxidine	272 ± 33	< 0.01	866 ± 542	NS	17.9 ± 1.9	< 0.01

1 Penicillin G and neomycin SO_4 were added at a level of 0.1% of the diet and sulfasuxidine at the 1% level.

2 Weight gain from the 7th to the 35th day of age.

3 Probability of value being different from respective unsupplemented control group, P greater than 0.05 taken as not significant (NS).

4 Mean for eight chicks ± standard deviation.

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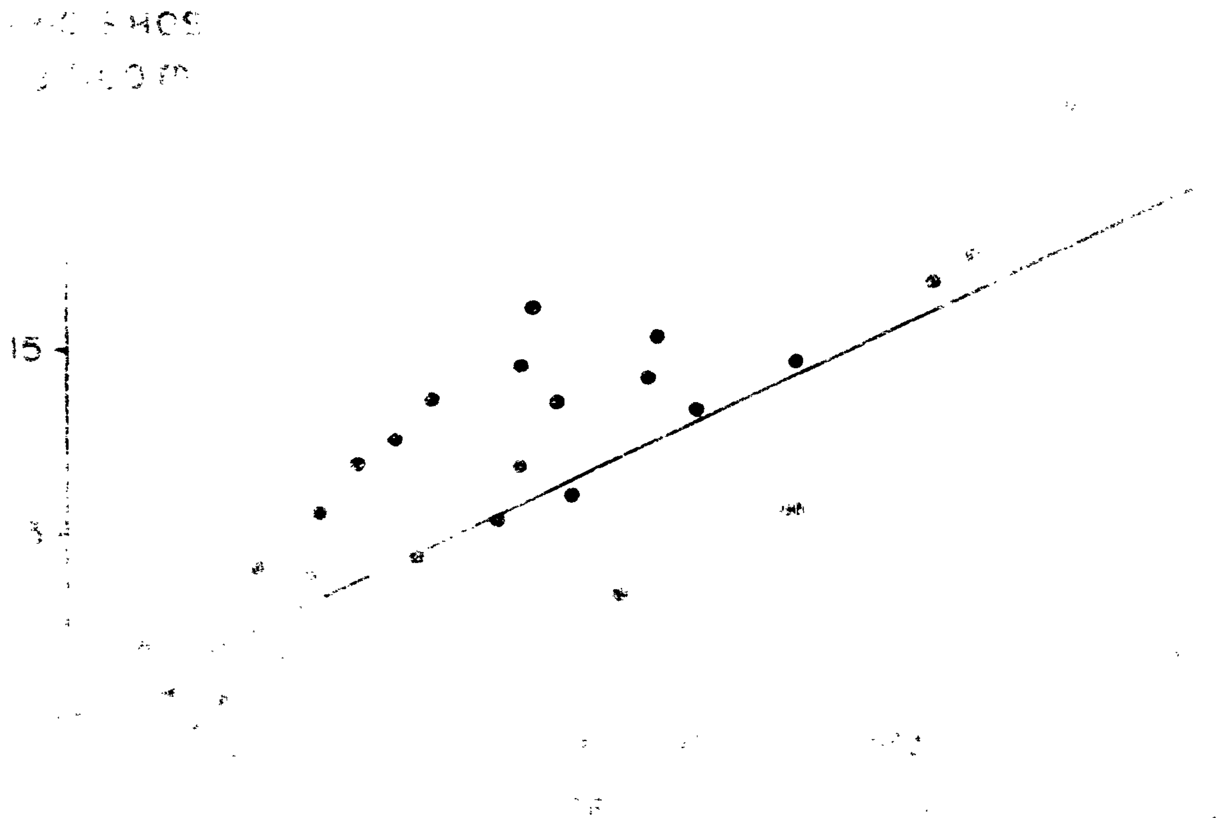
CORRELATION BETWEEN PLASMA CHOLESTEROL AND LIPID PHOSPHORUS IN CHICKS FED A CHOLESTEROL-FREE DIET



CORRELATION BETWEEN PLASMA CHOLESTEROL AND LIPID PHOSPHORUS IN CHICKS FED 2 % CHOLESTEROL

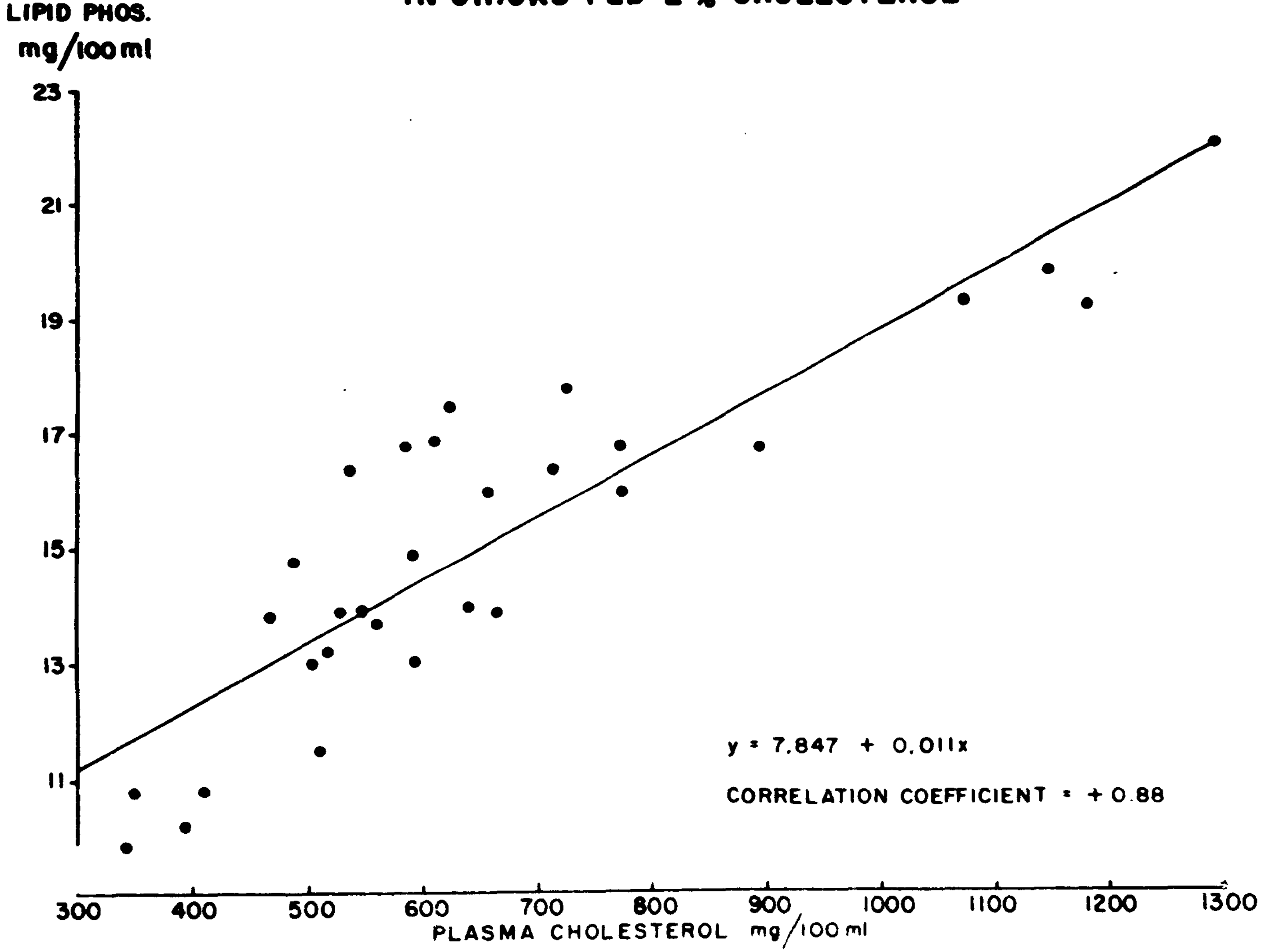


FIG. 2

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8 pp. 3 tables 2 figures 12 March 1963 UNCLASSIFIED

Growing chicks were fed semi-purified diets supplemented with antibiotics or sulfa drugs in the presence or absence of supplemental cholesterol. The data indicate that antibiotics and sulfa drugs depress plasma cholesterol levels of chicks fed a cholesterol-free diet when they also stimulate growth, but are without effect in the absence of such a growth stimulation. In cholesterol-fed chicks, antibiotics and sulfasuxidine elevated plasma cholesterol and lipid phosphorus levels. A highly significant positive correlation was observed between plasma cholesterol and lipid phosphorus levels for chicks fed either a cholesterol-free or supplemented diet.

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